AMENDMENTS TO THE CLAIMS

This listing of the claims replaces all prior versions and listings:

1. (Original) A controlled release pharmaceutical composition for oral administration of tolperisone to a subject comprising an amount of enantiomeric mixture of tolperisone, or pharmaceutically acceptable salts thereof, and a controlled release agent to provide for controlled release of the enantiomeric mixture of tolperisone upon such oral administration resulting in stereoselective disposition of tolperisone enantiomers in the blood plasma of the subject wherein the plasma area under the curve (AUC) concentration ratio of R- tolperisone to S-tolperisone is higher than that of a non-controlled release composition containing the same amount of enantiomeric mixture of tolperisone.

2. (Original) The controlled release pharmaceutical composition of claim 1 wherein the pharmaceutical composition further comprises (a) a core which includes (i) the enantiomeric mixture of tolperisone and (ii) the controlled release agent and (b) a controlled release coating associated with the core.

3. (Original) The controlled release pharmaceutical composition of claim 1 wherein the enantiomeric mixture of tolperisone is a racemic mixture.

4. (Original) The controlled release pharmaceutical composition of claim 3 wherein the amount of racemic mixture in the core is within the range of 100-249 mg.

5. (Original) The controlled release pharmaceutical composition of claim 1 wherein the controlled release of the racemic mixture of tolperisone results in no more than 55% by weight at 2 hours (measured using the USP Basket Method at 75 rpm in 1,000 ml 0.1 HCL at 37° C).

6. (Original) The controlled release pharmaceutical composition of claim 4 wherein the controlled release of the racemic mixture of tolperisone results in no more than 45% by weight at 2 hours (measured using the USP Basket Method at 75 rpm in 1,00O mI O-I HCL aI SV0 C).

7. (Original) The controlled release pharmaceutical composition of claim 3 wherein the amount of racemic mixture in the core is within the range of 250-500 mg.

8. (Original) The controlled release pharmaceutical composition of claim 7 wherein the composition exhibits an in vitro dissolution profile (measured using the USP Basket Method at 75 rpm in 1,000 ml 0.1 N HCL at 37° C) where after 2 hours no more than 20% (by weight) of the racemic mixture is released.

9. (Original) The controlled release pharmaceutical composition of claim 7 wherein the composition exhibits an in vitro dissolution profile (measured using the USP Basket Method at 75 rpm in 1,000 ml 0.1 N HCL at 37° C) where after 2 hours no more than 30% (by weight) of the racemic mixture is released.

10. (Original) The controlled release pharmaceutical composition of claim 7 wherein the composition further exhibits an in vitro dissolution profile (measured using the USP Basket Method at 75 rpm in 1 ,000 ml 0.1 N HCL at 37° C) where after 4 hours no more than 60% (by weight) of the racemic mixture has been released.

11. (Original) The controlled release pharmaceutical composition of claim 1 wherein the controlled release agent is a mixture of anionic and cationic acrylic polymers.

12. (Original) The controlled release pharmaceutical composition of claim 11 wherein said mixture of anionic and cationic acrylic polymers is a mixture of Eudragit RS, Eudragit L and Eudragit S.

13. (Original) The controlled release pharmaceutical composition of claim 1 wherein the controlled release coating is pH independent.

14. (Original) The controlled release pharmaceutical composition of claim 13 wherein the controlled release coating is Eudragit RS.

15. (Original) The controlled release pharmaceutical composition of claim 1 wherein the controlled release coating is pH dependent.

16. (Original) The controlled release pharmaceutical composition of claim 15 wherein the controlled release coating is Eudragit L.

17. (Original) A controlled release pharmaceutical composition for oral administration of tolperisone to a subject comprising an amount of racemic tolperisone, or pharmaceutically acceptable salts thereof, and a controlled release agent to provide for controlled release of the racemic tolperisone upon such oral administration resulting in stereoselective disposition of tolperisone enantiomers in the blood plasma of the subject wherein the plasma area under the curve (AUC) concentration ratio of R-tolperisone to S-tolperisone is 3 : 1 or higher.

18. (Original) The controlled release pharmaceutical composition of claim 17 wherein the pharmaceutical composition further comprises (a) a core which includes (i) the racemic mixture of tolperisone and (ii) the controlled release agent and (b) a controlled release coating associated with the core.

19. (Original) The controlled release pharmaceutical composition of claim 17 wherein the plasma area under the curve (AUC) concentration ratio is 4:1 or higher.

20. (Original) The controlled release pharmaceutical composition of claim 17 wherein the amount of racemic tolperisone is within the range of 100-249 mg.

21. (Original) The controlled release pharmaceutical composition of claim 20 wherein the controlled release of the racemic tolperisone results in no more than 55% by weight at 2 hours (measured using the USP Basket Method at 75 rpm in 1,000 ml 0.1 HCL at 37° C).

22. (Original) The controlled release pharmaceutical composition of claim 20 wherein the controlled release of the racemic tolperisone results in no more than 45% by weight at 2 hours (measured using the USP Basket Method at 75 rpm in 1,000 ml 0.1 HCL at 37° C).

23. (Original) The controlled release pharmaceutical composition of claim 17 wherein the amount of racemic tolperisone is within the range of 250-500 mg.

24. (Original) The controlled release pharmaceutical composition of claim 23 wherein the composition exhibits an in vitro dissolution profile (measured using the USP Basket Method at 75 rpm in 1 ,000 ml 0.1 N HCL at 37° C) where after 2 hours no more than 20% (by weight) of the racemic mixture is released.

25. (Original) The controlled release pharmaceutical composition of claim 23 wherein the composition exhibits an in vitro dissolution profile (measured using the USP Basket Method at 75 rpm in 1,000 ml 0.1 N HCL at 37° C) where after 2 hours no more than 30% (by weight) of the racemic tolperisone is released.

26. (Original) The controlled release pharmaceutical composition of claim 23 wherein the composition further exhibits an in vitro dissolution profile (measured using the USP Basket Method at 75 rpm in 1,000 ml 0.1 N HCL at 37° C) where after 4 hours no more than 60% (by weight) of the racemic tolperisone has been released.

27. (Original) The controlled release pharmaceutical composition of claim 17 wherein the controlled release agent is a mixture of anionic and cationic acrylic polymers.

28. (Original) The controlled release pharmaceutical composition of claim 27 wherein said mixture of anionic and cationic acrylic polymers is a mixture of Eudragit RS, Eudragit L and Eudragit S.

29. (Original) The controlled release pharmaceutical composition claim 17 wherein the controlled release coating is pH independent.

30. (Original) The controlled release pharmaceutical composition of claim 29 wherein the controlled release coating is Eudragit RS.

31. (Original) The controlled release pharmaceutical composition of claim 17 wherein the controlled release coating is pH dependent.

32. (Original) The controlled release pharmaceutical composition of claim 31 wherein the controlled release coating is Eudragit L.

33. (Original) A method of oral administration of tolperisone to a subject comprising: oral administration by controlled release of a dose of an amount of racemic tolperisone in the range of 100-500 mg to provide a stereoselective disposition of tolperisone enantiomers in the blood plasma of the subject.

34. (Original) The method of claim 33 wherein the amount of racemic tolperisone is in the range of about 300 mg.

35. (Original) The method of claim 33 wherein the amount of racemic tolperisone is in the range of about 150 mg.

36. (Original) The method of claim 33 wherein the amount of racemic tolperisone is in the range of 250-350 mg and the stereoselective disposition of tolperisone enantiomers in the blood plasma of the subject has a plasma area under the curve (AUC) concentration of R-tolperisone of 100 ng*h/ml or higher and such concentration for S-tolperisone is 25 ng*h/ml or lower.

37. (Original) A controlled release pharmaceutical composition comprising racemic tolperisone in the amount of 100-200 mg, or pharmaceutically acceptable salts thereof, wherein the composition exhibits an in vitro dissolution profile (measured using the USP Basket Method at 75 rpm in 1,000 ml 0.1 N HCL at 37 ° C) where after 2 hours no more than 45% (by weight) of the racemic tolperisone is released.

38. (Original) The controlled release pharmaceutical composition of claim 37 wherein the composition exhibits an in vitro dissolution profile (measured using the USP Basket Method at 75 rpm in 1,000 ml 0.1 N HCL at 37° C) where after 2 hours no more than 55% (by weight) of the racemic tolperisone is released.

39. (Original) The controlled release pharmaceutical composition of claim 37 wherein the composition further comprises: a core including the racemic tolperisone, or pharmaceutically acceptable salts thereof, and a controlled release agent; and a controlled release coating associated with the core.

40. (Original) The controlled release pharmaceutical composition of claim 39 wherein the composition provides upon oral administration to a subject for controlled release of the racemic tolperisone resulting in stereoselective disposition of tolperisone enantiomers in the blood plasma of the subject.

41. (Original) A controlled release pharmaceutical composition comprising racemic tolperisone in the amount of 201-500 mg, or pharmaceutically acceptable salts thereof, wherein

the composition exhibits an in vitro dissolution profile (measured using the USP Basket Method at 75 rpm in 1 ,000 ml 0.1 N HCL at 37° C) where after 2 hours no more than 20% (by weight) of the racemic mixture is released.

42. (Original) The controlled release pharmaceutical composition of claim 41 wherein the composition exhibits an in vitro dissolution profile (measured using the USP Basket Method at 75 rpm in 1,000 ml 0.1 N HCL at 37° C) where after 2 hours no more than 30% (by weight) of the racemic tolperisone is released.

43. (Original) The controlled release pharmaceutical composition of claim 42 wherein the composition further exhibits an in vitro dissolution profile (measured using the USP Basket Method at 75 rpm in 1,000 ml 0.1 N HCL at 37° C) where after 4 hours no more than 60% (by weight) of the racemic tolperisone has been released.

44. (Original) The controlled release pharmaceutical composition of claim 41 wherein the composition further comprises: a core including the racemic tolperisone, or pharmaceutically acceptable salts thereof, and a controlled release agent; and a controlled release coating associated with the core.

45. (Original) The controlled release pharmaceutical composition of claim 44 wherein the composition provides upon oral administration to a subject for controlled release of the racemic tolperisone resulting in stereoselective disposition of tolperisone enantiomers in the blood plasma of the subject.

46. (Currently amended) A method of treating a chronic disease, benefiting from administration of a muscle relaxant, comprising ~~the administration of any of~~ administering the pharmaceutical ~~compositions~~ composition of ~~claims 1-32, 37-45 and 59-62~~ claim 1 to a subject in need thereof.

47. (Original) The method of claim 46 wherein the chronic disease is selected from the group consisting of multiple sclerosis, fibromyalgia, Parkinson's disease, climacteric symptoms, spasticity resulting from a stroke, spasticity resulting from neurological diseases, cervical syndrome, lumbago, cervico-brachial syndrome, osteoporosis, arthritis, rheumatic diseases such as soft tissue rheumatism and chronic polyarthritis.

48. (Original) The method of claim 47 wherein the chronic disease is multiple sclerosis.

49. (Original) The method of claim 47 wherein the chronic disease is spasticity resulting from a stroke.

50. (Original) The method of claim 47 wherein the chronic disease is spasticity resulting from neurological diseases.

51. (Original) The method of claim 47 wherein the chronic disease is fibromyalgia.

52. (Original) The method of claim 47 wherein the chronic disease is Parkinson's disease.

53. (Original) The method of claim 47 wherein the chronic disease is climacteric symptoms.

54. (Original) The method of claim 47 wherein the chronic disease is cervical syndrome.

55. (Original) The method of claim 47 wherein the chronic disease is cervico-brachial syndrome.

56. (Original) The method of claim 47 wherein the chronic disease is osteoporosis.

57. (Original) The method of claim 47 wherein the chronic disease is arthritis.

58. (Original) The method of claim 47 wherein the chronic disease is rheumatic diseases such as soft tissue rheumatism and chronic polyarthritis.

59. (Original) A controlled release pharmaceutical composition for oral administration to a subject of tolperisone comprising: a core including about 125-175 mg of racemic tolperisone, or pharmaceutically acceptable salts thereof, and a controlled release agent comprising a homogeneous mixture of about 9-12 mg of Eudragit S, about 1.5-2.25 mg Eudragit RS and about 9-12 mg Eudragit L; and a controlled release coating comprising about 1-4 mg Eudragit L associated with the core to provide for controlled release of the racemic tolperisone upon such

oral administration resulting in stereoselective disposition of tolperisone enantiomers in the blood plasma of the subject.

60. (Original) The controlled release table of claim 59 wherein the controlled release agent comprises a homogeneous mixture of about 10.5 mg Eudragit S, about 1.88 mg Eudragit RS and about 105 mg Eudragit L and the controlled release coating comprises about 2 mg Eudragit L.

61. (Original) A controlled release pharmaceutical composition for oral administration to a subject of tolperisone comprising: a core including about 300 mg of racemic tolperisone, or pharmaceutically acceptable salts thereof, and a controlled release agent comprising a homogeneous mixture of about 2.5-5 mg Eudragit RS, about 20- 22 mg Eudragit L and about 20-22 mg Eudragit S; and a controlled release coating comprising about 4-10 mg Eudragit RS associated with the core to provide for controlled release of the racemic tolperisone upon such oral administration resulting in stereoselective disposition of tolperisone enantiomers in the blood plasma of the subject.

62. (Original) The controlled release pharmaceutical composition of claim 51 wherein the controlled release agent comprises about 3.75 mg Eudragit RS, about 21 mg Eudragit L and about 21 mg Eudragit S and the controlled release coating comprises about 4.5 mg of Eudragit RS.

63. (Original) A controlled release pharmaceutical composition for the oral administration of racemic tolperisone to a subject in need thereof comprising racemic toleprisone in a pharmaceutical carrier comprising a mixture of hydrophilic polymers selected from the group consisting of anionic polymers and cationic polymers and derivatives thereof and combinations thereof dispersed in a hydrophobic matrix.

64. (Original) The composition of claim 63 wherein the hydrophilic polymer is selected from the group consisting of Eudragit S anionic copolymer of methacrylic acid and methacrylic acid methyl ester, Eudragit E cationic copolymer of dimethylaminoethyl methacrylate and neutral methacrylic acid esters, Eudragit RL copolymer of methacrylic acids, Eudragit RS copolymer of methacrylic acids, methacrylic acid polymer, hydroxyethyl methacrylic acid polymer and hydroxymethyl methacrylic acid polymer.

65. (Original) The composition of claim 63 wherein the hydrophobic component is selected from the group consisting of glyceryl dibehenate, glyceryl monostearate, mixtures of glyceryl monostearate and glyceryl monopal reitate, glycerylmonooleate, mixtures of mono, di and tri-glycerides, glycerylmonolaurate, paraffin, white wax, long chain carboxylic acids, long chain carboxylic acid esters and long chain carboxylic acid alcohols.

66. (Original) A controlled release formulation of racemic tolperisone for oral administration comprising: an effective amount of racemic tolperisone, a hydrophobic material, and a water sensitive material.

67. (Original) The composition of claim 66 wherein the water sensitive material is a hydrophilic polymer selected from the group consisting of Eudragit S anionic copolymer of methacrylic acid and methacrylic acid methyl ester, Eudragit E cationic copolymer of dimethylaminoethyl methacrylate and neutral methacrylic acid esters, Eudragit RL copolymer of methacrylic acids, Eudragit RS copolymer of methacrylic acids, methacrylic acid polymer, hydroxyethyl methacrylic acid polymer and hydroxymethyl methacrylic acid polymer.

68. (Original) The composition of claim 66 wherein the hydrophobic material is selected from the group consisting of glyceryl dibehenate, glyceryl monostearate, mixtures of glyceryl monostearate and glyceryl monopal reitate, glycerylmonooleate, mixtures of mono, di and tri-glycerides, glycerylmonolaurate, paraffin, white wax, long chain carboxylic acids, long chain carboxylic acid esters and long chain carboxylic acid alcohols.

69. (Original) The controlled release pharmaceutical composition of claim 1 wherein the enantiomeric mixture of tolperisone has at least 50 % by weight the R-tolperisone and no less than 10 % by weight the S-tolperisone.

70. (New) A method of treating a chronic disease, benefiting from administration of a muscle relaxant, comprising administering the pharmaceutical composition of claim 1 to a subject in need thereof.

71. (New) A method of treating a chronic disease, benefiting from administration of a muscle relaxant, comprising administering the pharmaceutical composition of claim 17 to a subject in need thereof.

72. (New) A method of treating a chronic disease, benefiting from administration of a muscle relaxant, comprising administering the pharmaceutical composition of claim 37 to a subject in need thereof.

73. (New) A method of treating a chronic disease, benefiting from administration of a muscle relaxant, comprising administering the pharmaceutical composition of claim 41 to a subject in need thereof.

74. (New) A method of treating a chronic disease, benefiting from administration of a muscle relaxant, comprising administering the pharmaceutical composition of claim 59 to a subject in need thereof.

75. (New) A method of treating a chronic disease, benefiting from administration of a muscle relaxant, comprising administering the pharmaceutical composition of claim 61 to a subject in need thereof.

76. (New) A method of treating a chronic disease, benefiting from administration of a muscle relaxant, comprising administering the pharmaceutical composition of claim 63 to a subject in need thereof.

77. (New) A method of treating a chronic disease, benefiting from administration of a muscle relaxant, comprising administering the pharmaceutical composition of claim 66 to a subject in need thereof.